

MNA			
4-Hydroxyphenylacetyl-Pro-Ala-Gly-Pro-MNA	0.69	1.72	10
Succinyl-Pro-Ala-Gly-Pro-MNA	0.29	1.44	11
Glutaryl-Pro-Ala-Gly-Pro-MNA	0.3	1.48	12
2-Morpholino-ethyl-Pro-Ala-Gly-Pro-MNA	0.26	0.64	13
Morpholino-carbonyl-Pro-Ala-Gly-Pro-MNA	0.6	2.99	14
Morpholino-(ethyloxycarbonyl)-Pro-Ala-Gly-Pro-MNA	0.65	3.25	15
4-Dimethylaminobenzoyl-Pro-Ala-Gly-Pro-MNA	0.37	1.85	16
Prazin-2-ylcarbonyl-Pro-Ala-Gly-Pro-MNA	0.56	0.7	17
1-Methylpyrrol-2-ylcarbonyl Pro-Ala-Gly-Pro-MNA	0.13	0.33	18
Malonyl-Pro-Ala-Gly-Pro-MNA	0.21	1.05	19
3-Carboxyphenylsulfonyl-Pro-Ala-Gly-Pro-MNA	0.58	2.88	20
Pyrid-4-ylmethyloxycarbonyl-Pip-Ala-Gly-Pro-MNA <sup>1</sup>	0.43	2.16	
Pyrid-4-ylmethyloxycarbonyl-2-Aze-Ala-Gly-Pro-MNA <sup>2</sup>	1.61	8.07	
Pyrid-3-ylmethyloxycarbonyl-Pip-Ala-Gly-Pro-MNA <sup>1</sup>	0.56	2.78	
Pyrid-3-ylmethyloxycarbonyl-MeAla-Ala-Gly-Pro-MNA <sup>3</sup>	1.27	6.31	
Pyrid-3-ylmethyloxycarbonyl-2-Aze-Ala-Gly-Pro-MNA <sup>2</sup>	3.42	17.1	

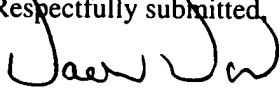
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#### REMARKS

Attached hereto is a computer readable form of the sequence listing, a paper copy including the amendment directing its entry into the specification and a statement under 37 C.F.R. 1.821(f). No new matter has been added to this application by way of amendment. Entry of this amendment is respectfully requested.

Also attached hereto is a marked up version of the changes made to the specification by the current amendment. The attached pages are captioned "Versions with Marking to Show Changes Made".

Respectfully submitted,



David Dow  
Reg. 46,124

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to:

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Assistant Commissioner for Patents  
Washington, DC 20231

on June 11, 2002



By: David Dow  
Reg. No. 46,124

Patent Department  
Boehringer Ingelheim Corp.  
900 Ridgebury Road  
P.O. Box 368  
Ridgefield, CT. 06877  
Tel.: (203) 791-6764

### Versions with Marking to Show Changes Made

At page 3 paragraph two has be rewritten as follows:

The International patent applications WO 97/12624 and WO 97/14416 disclose oligopeptides including the following penta- and hexapeptide (SEQ. ID NOs.: 151 and 177: ~~hArg-eTyr-Gln-SER-Pro hArg-Typr-Gln-Ser-Pro~~), comprising amino acid sequences, which are recognized and proteolytically cleaved by free prostate specific antigen (PSA) and therapeutic agents which comprise conjugates of such oligopeptides and known therapeutic or cytotoxic agents. These oligopeptide conjugates which comprise at least one glutamic-serine moiety are useful for treatment of prostate cancer only

At page 8 the last paragraph has been re-written as follows:

Most preferred are the compounds of formula I, wherein R<sup>1</sup> is a group selected from the formulae (1) to (14):

Cg-Gly	(15)	
Cg-Nle	(16)	
Cg-Val	(17)	
Cg-Met	(18)	
Cg-Xxx-Gly	(19)	
Cg-Xxx-Hyn	(20)	
Cg-Xxx-Pro	(21)	
Cg-Xxx-His	(22)	
Cg-Xxx-Met	(23)	
Cg-Xxx-Ala	(24)	
Cg-Xxx-Hyn	(25)	
Cg-Xxx-Ala-Gly	(26)	
Cg-(Xxx) <sub>n</sub> -Xxx-Gly	(27)	<u>SEQ.ID NO.: 1</u>
Cg-(Xxx) <sub>n</sub> -Xxx-Ala-Gly	(28)	<u>SEQ. ID NO.: 2</u>

wherein

Cg represents a capping group selected from pyridinyloxycarbonyl, pyridinylacetyl, pyridinylmethylsulfonyl and pyridylmethylaminocarbonyl;  
 Xxx represents a moiety derived from an amino carboxylic acid; and  
 n is an integer from 1 to 6. –

At page 28 please replace the first paragraph with the following re-written paragraph:

Example 7

**Synthesis of Pyridin-3-ylmethoxycarbonyl-Pro-Ala-Gly-Pro-OH (SEQ.ID NO.: 3)**

At page 30 the last paragraph has been rewritten as follows:

Example 21

**Synthetic procedures of doxorubicin conjugates**

**21** Pyridin-3-ylmethoxycarbonyl-Pro-Ala-Gly-Pro-Doxorubicin (SEQ. ID. NO: 4)  
 Pyridin-3-ylmethoxycarbonyl-Pro-Ala-Gly-Pro-OH (SEQ. ID. NO.: 3) (180.7 mg, 0.38 mmol) and N-hydroxysuccinimide (44 mg, 0.37 mmol) were weighed out and placed in a 2 neck-round bottom flask under dinitrogen. Anhydrous *N,N*-dimethylformamide (20 ml) was added and the flask was cooled to 0 °C in an ice bath. Dicyclohexylcarbodiimide (78 mg, 0.38 mmol) was added as a 1 ml solution in *N,N*-dimethylformamide. The solution was stirred at 0 °C for 40 minutes.

At page 41 the third paragraph has been re-written as follows:

Example 56

**Synthesis of Pyridin-3-ylmethoxycarbonyl-Pro-Ala-Gly-Pro-MNA (SEQ. ID. NO. 5)**

At page 42 please the first paragraph has been re-written as follows:

MNA-Conjugate	% Turnover	Cleavage [μM]	<u>SEQ. ID NO.</u>
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4-Amino-Phenylacetyl-Gly-Pro-MNA	0.6	3	
3,5-Difluorophenylacetyl-Gly-Pro-MNA	2.26	2.26	
2-Fluorophenylacetyl-Gly-Pro-MNA	0.26	1.28	
3-Fluorophenylacetyl-Gly-Pro-MNA	0.35	1.77	
4-Fluorophenylacetyl-Gly-Pro-MNA	0.42	2.08	
3-Pyridylacetyl-Gly-Pro-MNA	1.82	9.12	
3-Pyridylmethyloxycarbonyl-Gly-Pro-MNA	0.72	3.58	
4-Pyridylmethyloxycarbonyl-Gly-Pro-MNA	1.18	5.92	
3-Pyridylmethyloxycarbonyl-Pro-Ala-Gly-Pro-MNA	1.77	8.86	<u>5</u>
4-Pyridylmethyloxycarbonyl-Pro-Ala-Gly-Pro-MNA	1.28	6.38	<u>6</u>
4-Aminomethylbenzoyl-Pro-Ala-Gly-Pro-MNA	0.24	1.21	<u>7</u>
4-Aminomethylphenylacetyl-Pro-Ala-Gly-Pro-MNA	0.26	1.28	<u>8</u>
4-(2-Aminothiazol-5-yl)-acetyl-Pro-Ala-Gly-Pro-MNA	0.39	1.94	<u>9</u>
4-Hydroxyphenylacetyl-Pro-Ala-Gly-Pro-MNA	0.69	1.72	<u>10</u>
Succinyl-Pro-Ala-Gly-Pro-MNA	0.29	1.44	<u>11</u>
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